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|---------------|-------------|----------------------|---------------------|
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RADIO, S. EXAMINER

18N2/0720

FLEHR, HOHBACH, TEST  
ALBRITTON & HERBERT  
SUITE 3400  
FOUR EMBARCADERO CENTER  
SAN FRANCISCO, CA 94111-4187

| ART UNIT | PAPER NUMBER |
|----------|--------------|
| 1808     | 13           |

DATE MAILED: 07/20/94

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 4/1/94 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.  
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

**Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:**

- |   |  |
|---|--|
| 1. <input type="checkbox"/> Notice of References Cited by Examiner, PTO-892.        | 2. <input type="checkbox"/> Notice re Patent Drawing, PTO-948.                   |
| 3. <input type="checkbox"/> Notice of Art Cited by Applicant, PTO-1449.             | 4. <input type="checkbox"/> Notice of Informal Patent Application, Form PTO-152. |
| 5. <input type="checkbox"/> Information on How to Effect Drawing Changes, PTO-1474. | 6. <input type="checkbox"/>  |

**Part II SUMMARY OF ACTION**

1. ☒ Claims 1-13 are pending in the application.  
Of the above, claims \_\_\_\_\_ are withdrawn from consideration.
2. ☐ Claims \_\_\_\_\_ have been cancelled.
3. ☐ Claims \_\_\_\_\_ are allowed.
4. ☒ Claims 1-13 are rejected.
5. ☐ Claims \_\_\_\_\_ are objected to.
6. ☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.
7. ☐ This application has been filed with Informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on \_\_\_\_\_. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on \_\_\_\_\_ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on \_\_\_\_\_, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received  
☐ been filed in parent application, serial no. \_\_\_\_\_; filed on \_\_\_\_\_.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

The amendment filed on April 1, 1994 is acknowledged and has been entered. Claims 1-13 are currently pending in the instant application and have been examined on the merits.

Claims 1-13 remain rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 11 and 12 remain rejected for lacking proper antecedent basis for the phrase "the tissue".

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered

therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1-10 remain rejected under 35 U.S.C. § 103 as being unpatentable over Reynolds et al (Rest. <sup>R1</sup> Neuro. & Neurosci.) in view of Masters et al.

Reynolds et al teach isolating neural stem cells from a donor tissue and proliferating the stem cells by culturing the cells in a medium comprising EGF. The EGF-generated progenitor cells were differentiated by culturing the stem cells in a second medium in the absence of EGF.

Reynolds et al differs slightly from the claimed invention by not adding a second growth factor to the second culture medium.

However, Masters et al teaches that growth factors such as IGF-I accelerates the differentiation of neural cells into differentiated neural cells. Thus it would have been obvious to one of ordinary skill in the art to add a growth factor which is known to accelerate the differentiation of neural cells to the culture which is already differentiating in the absence of EGF.

Accordingly, the claimed invention would have been prima facie obvious to one of ordinary skill in the art at the time the

claimed invention was made, especially in the absence of sufficient, clear and convincing evidence to the contrary.

Claims 1-10 remain rejected under 35 U.S.C. § 103 as being unpatentable over Cattaneo et al (Letters to Nature) taken with  
5    2 Reynolds et al (Soc. for Neurosci. Ab.) or Anchan et al (J. Cell. Biol.) and further in view of Masters et al.

Cattaneo et al teaches culturing neural stems in a medium containing bFGF and then culturing the stem cells in a medium containing bFGF and NGF in order to proliferate the stem cells.  
10    The stem cells proliferate in response to NGF but only after they have been exposed to bFGF. The number of cells in the culture which proliferates is increased as a result of this pre-exposure to bFGF and further culturing in bFGF and NGF. Cattaneo et al proceeds to discuss that when the growth factors are removed the  
15    cells differentiate.

Cattaneo et al differs from the claimed invention by proliferating the stem cells in the second culture medium which comprises bFGF and NGF. The instant claims proliferate the stem cells in the second culture medium which comprises bFGF and EGF.

20    Reynolds et al teach that culturing neural precursor cells in a medium comprising EGF or TGF causes said cells to proliferate and produce precursor cells.

Anchan et al also teaches that EGF or NGF increases neural cell proliferation in a dose-dependent manner.

25    Therefore, it would have been obvious to one of ordinary

skill in the art to substitute one well known neural cell proliferation growth factor for another and have a reasonable expectation of success. In fact Anchan et al teaches that EGF and NGF have the same effect on neural cells thus providing the skilled artisan with the proper motivation to substitute the EGF, taught by Reynolds et al or Anchan et al, for the NGF, taught in the process of Cattaneo.

Furthermore, the skilled artisan would have a reasonable expectation success in proliferating said neural cells in the methods of Cattaneo et al taken with Reynolds et al or Anchan et al. As decided in In re O'Farrel (7 USPQ 2d, 1673-1681, Fed. Cir. 1988), obviousness does not require absolute predictability of success. Indeed, for many inventions that seem quite obvious, there is no absolute predictability of success until the invention is reduced to practice. There is always at least a possibility of unexpected results, that would then provide an objective basis for showing that the invention, although apparently obvious, was in law nonobvious. In re Merck & Co., 800 F.2d at 1098, 231 USPQ at 380; Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co., 730 F.2d 1452, 1461, 221 USPQ 481, 488 (Fed. Cir. 1984); In re Papesch, 315 F.2d 381, 386-387, 137 USPQ 43, 47-48 (CCPA 1963). For obviousness under 35 U.S.C. 103, all that is required is a reasonable expectation of success. In re Longi, 759 F.2d 887, 897, 225 USPQ 645, 651-652 (Fed. Cir. 1985); In re Clinton, 527 F.2d 1226, 1228, 188 USPQ 365, 367

(CCPA 1976).

Cattaneo et al also differs slightly from the claimed invention by not adding a second growth factor to the second culture medium.

5           However, Masters et al teaches that growth factors such as IGF-I accelerates the differentiation of neural cells into differentiated neural cells. Thus it would have been obvious to one of ordinary skill in the art to add a growth factor which is known to accelerate the differentiation of neural cells to the  
10           culture which is already differentiating in the absence of the growth factors which induced proliferation.

          Accordingly, the claimed invention would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made, especially in the absence of  
15           sufficient, clear and convincing evidence to the contrary.

          Claim 11 remains rejected under 35 U.S.C. § 103 as being unpatentable over Cattaneo et al (Letters to Nature) taken with Reynolds et al (Soc. for Neurosci. Ab.) or Anchan et al (J. Cell. Biol.).

20           The references are relied upon as discussed supra.

          Accordingly, the claimed invention would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made, especially in the absence of sufficient, clear and convincing evidence to the contrary.

25           Claims 12-13 remain rejected under 35 U.S.C. § 103 as being

unpatentable over Gensburger et al taken with Yamada et al.

Gensburger et al teaches a method of isolating neural cells from the tissue of a donor and culturing the cells in a culture medium comprising a growth factor which stimulates proliferation of the neural precursor cells in vitro.

Gensburger et al does <sup>not</sup> continue to teach the differentiation of the precursor cells by contacting the cells with a substrate. However, Yamada et al teaches that as a component of the extracellular matrix, fibronectin, is well known in the art to modulate the differentiation of a variety of cell types. For example, fibronectin is known to differentiate neural cells. Therefore, one of ordinary skill in the art would have a reasonable expectation of using fibronectin as the substrate to differentiate neural precursor cells.

Thus it would have been obvious to one of ordinary skill in the art to proliferate the neural cells by culturing the isolated cells in a medium comprising a growth factor such as bFGF and continuing to differentiate the cells which were proliferated by contacting them to a substrate such as fibronectin.

Accordingly, the claimed invention would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made, especially in the absence of sufficient, clear and convincing evidence to the contrary.

No claim is allowed.

This is a file-wrapper continuation of applicant's earlier

Serial No. 07/967,622  
Art Unit 1808


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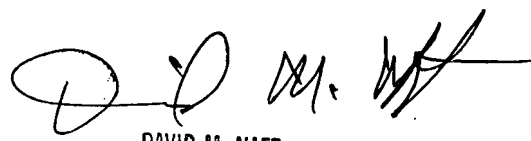
application S.N. 07/967,622. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds or art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See M.P.E.P. § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). The practice of automatically extending the shortened statutory period an additional month upon the filing of a timely first response to a final rejection has been discontinued by the Office. See 1021 TMOG 35.

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Susan M. Dadio whose telephone number is (703) 308-2392.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

  
Susan M. Dadio  
July 15, 1994

  
DAVID M. NAFF  
PRIMARY EXAMINER  
ART UNIT 1826